

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
7 June 2001 (07.06.2001)

PCT

(10) International Publication Number
WO 01/40466 A3

(51) International Patent Classification ⁷ :	C12N 15/12, C07K 14/47, 14/705, C12N 15/62, C07K 16/18, 16/28, G01N 33/53, A61K 38/17, C12Q 1/68	PCT/US99/30911 20 December 1999 (20.12.1999) US
(21) International Application Number:	PCT/US00/32678	PCT/US99/30999 20 December 1999 (20.12.1999) US
(22) International Filing Date:	1 December 2000 (01.12.2000)	PCT/US99/31243 30 December 1999 (30.12.1999) US
(25) Filing Language:	English	PCT/US99/31274 30 December 1999 (30.12.1999) US
(26) Publication Language:	English	PCT/US00/00219 5 January 2000 (05.01.2000) US
(30) Priority Data:		PCT/US00/00277 6 January 2000 (06.01.2000) US
	PCT/US99/28301 1 December 1999 (01.12.1999) US	PCT/US00/00376 6 January 2000 (06.01.2000) US
	PCT/US99/28634 1 December 1999 (01.12.1999) US	PCT/US00/03565 11 February 2000 (11.02.2000) US
	PCT/US99/28551 2 December 1999 (02.12.1999) US	PCT/US00/04341 18 February 2000 (18.02.2000) US
	PCT/US99/28564 2 December 1999 (02.12.1999) US	PCT/US00/04342 18 February 2000 (18.02.2000) US
	PCT/US99/28565 2 December 1999 (02.12.1999) US	PCT/US00/04414 22 February 2000 (22.02.2000) US
	60/170,262 9 December 1999 (09.12.1999) US	PCT/US00/04914 24 February 2000 (24.02.2000) US
	PCT/US99/30095 16 December 1999 (16.12.1999) US	PCT/US00/05004 24 February 2000 (24.02.2000) US
		PCT/US00/05601 1 March 2000 (01.03.2000) US
		PCT/US00/05841 2 March 2000 (02.03.2000) US

[Continued on next page]

(54) Title: SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

MSTMFADTLLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKETITESAGR
QQKKKIERQEEKLKNNNRDLSMVRMKSMAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ
GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 53-57

(57) Abstract: The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

WO 01/40466 A3



60/187,202	3 March 2000 (03.03.2000)	US
PCT/US00/06319	10 March 2000 (10.03.2000)	US
PCT/US00/06884	15 March 2000 (15.03.2000)	US
PCT/US00/07377	20 March 2000 (20.03.2000)	US
PCT/US00/07532	21 March 2000 (21.03.2000)	US
PCT/US00/08439	30 March 2000 (30.03.2000)	US
PCT/US00/13705	17 May 2000 (17.05.2000)	US
PCT/US00/14042	22 May 2000 (22.05.2000)	US
PCT/US00/14941	30 May 2000 (30.05.2000)	US
PCT/US00/15264	2 June 2000 (02.06.2000)	US
60/209,832	5 June 2000 (05.06.2000)	US
PCT/US00/20710	28 July 2000 (28.07.2000)	US
PCT/US00/22031	11 August 2000 (11.08.2000)	US
PCT/US00/23522	23 August 2000 (23.08.2000)	US
PCT/US00/23328	24 August 2000 (24.08.2000)	US
60/000,000	15 September 2000 (15.09.2000)	US
PCT/US00/30952	8 November 2000 (08.11.2000)	US
PCT/US00/30873	10 November 2000 (10.11.2000)	US

(71) **Applicant (for all designated States except US):** GENENTECH, INC. [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(72) **Inventors; and**

(75) **Inventors/Applicants (for US only):** BAKER, Kevin, P. [GB/US]; 14006 Indian Run Drive, Darnestown, MD 20878 (US). BERESINI, Maureen [US/US]; 611 Stetson Street, Moss Beach, CA 94038 (US). DEFORGE, Laura [US/US]; 1175 Manzanita Drive, Pacifica, CA 94044 (US). DESNOYERS, Luc [CA/US]; 2050 Stockton Street, San Francisco, CA 94133 (US). FILVAROFF, Ellen [US/US]; 538 18th Avenue, San Francisco, CA 94121 (US). GAO, Wei-Qiang [CN/US]; 641 Pilgrim Drive, Foster City, CA 94404 (US). GERRITSEN, Mary, E. [CA/US]; 541 Parrott Drive, San Mateo, CA 94402 (US). GODDARD, Audrey [CA/US]; 110 Congo Street, San Francisco, CA 94131 (US). GODOWSKI, Paul, J. [US/US]; 2627 Easton Drive, Burlingame, CA 94010 (US). GURNEY, Austin, L. [US/US]; 1 Debbie Lane, Belmont, CA 94002

(US). SHERWOOD, Steven [US/US]; 995 Lundy Lane, Los Altos, CA 94024 (US). SMITH, Victoria [AU/US]; 19 Dwight Road, Burlingame, CA 94010 (US). STEWART, Timothy, A. [US/US]; 465 Douglass Street, San Francisco, CA 94114 (US). TUMAS, Daniel [US/US]; 3 Rae Avenue, Orinda, CA 94563 (US). WATANABE, Colin, K. [US/US]; 128 Corliss Drive, Moraga, CA 94556 (US). WOOD, William, I. [US/US]; 35 Southdown Court, Hillsborough, CA 94010 (US). ZHANG, Zemin [CN/US]; 876 Taurus Drive, Foster City, CA 94404 (US).

(74) **Agents:** KRESNAK, Mark, T. et al.; Genentech, Inc., MS49, 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(81) **Designated States (national):** AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) **Date of publication of the international search report:**
10 May 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

Inte: International Application No

PCT/US 00/32678

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C12N15/12	C07K14/47	C07K14/705	C12N15/62	C07K16/18
	C07K16/28	G01N33/53	A61K38/17	C12Q1/68	

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 21328 A (KATO SEISHI ;PROTEGENE INC (JP); SEKINE SHINGO (JP); SAGAMI CHEM R) 22 May 1998 (1998-05-22) * see seq.ID's.12, 37 and 62: clone HP10122 * --- WO 99 09061 A (GENETICS INST) 25 February 1999 (1999-02-25) * see clone am910_li * ---	1-20, 69-71
X		1-20 -/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

8 August 2001

Date of mailing of the international search report

12.11.01

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

INTERNATIONAL SEARCH REPORT

Interr	nat Application No
PCT/US 00/32678	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IWAMURO SHAWICHI ET AL: "Multi-ubiquitination of a nascent membrane protein produced in a rabbit reticulocyte lysate." JOURNAL OF BIOCHEMISTRY (TOKYO), vol. 126, no. 1, July 1999 (1999-07), pages 48-53, XP002174228 ISSN: 0021-924X the whole document ---	1-20
X	DATABASE EMBL [Online] Entry/Acc.no. AF070626, 2 July 1998 (1998-07-02) ANDERSON, B ET AL.: "Homo sapiens clone 24483 unknown mRNA, parital cds." XP002174229 the whole document ---	1-20
A	EP 0 834 563 A (SMITHKLINE BEECHAM CORP) 8 April 1998 (1998-04-08) the whole document ---	
A	WO 97 07198 A (GENETICS INST) 27 February 1997 (1997-02-27) the whole document ---	
A	KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, no. 93, 1 July 1996 (1996-07-01), pages 7108-7113, XP002077277 ISSN: 0027-8424 the whole document ---	
A	YOKOYAMA-KOBAYASHI M ET AL: "A signal sequence detection system using secreted protease activity as an indicator" GENE,NL,ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, vol. 163, no. 2, 3 October 1995 (1995-10-03), pages 193-196, XP004041983 ISSN: 0378-1119 the whole document ---	
P,X	WO 00 37630 A (GENETICS INST) 29 June 2000 (2000-06-29) * see clone AM910_1i * -----	1-13, 17-20

INTERNATIONAL SEARCH REPORT

I. International application No.
PCT/US 00/32678

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-20 and 69-71, all partially

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-20 and 69-71, all partially

PRO177: nucleic acid with seq.ID.1, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.2 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.2 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide.

Inventions 2-242: claims 1-20 and 69-71, all partially

Subject matter as defined for invention 1, but related to the respective nucleic acid/polypeptide sequences of:

Invention 2: PRO3574, represented by seq.ID.s 3 and 4,

Invention 3: PRO1280, represented by seq.ID.s 5 and 6,

Invention 4: PRO4984, represented by seq.ID's 7 and 8,

...
Invention 15: PRO1471, represented by seq.ID.s 29 and 30, (PRO1114 skipped; follows below)

Invention 16: PRO1076, represented by seq.ID.s 33 and 34, ...

Invention 92: PRO4345, represented by seq.ID.s 185 and 186, (PRO4978 skipped; follows below)

Invention 93: PRO4327, represented by seq.ID.s 221 and 222,

...
Invention 107: PRO6028, represented by seq.ID.s 217 and 218, (PRO100 skipped; follows below)

Invention 108: PRO4327, represented by seq.ID.s 221 and 222,

...
Invention 132: PRO197, represented by seq.ID.s 269 and 270, (PRO195 skipped; follows below)

Invention 133: PRO187, represented by seq.ID.s 273 and 274, (PRO182 skipped; follows below)

Invention 134: PRO188, represented by seq.ID.s 277 and 278,

...
Invention 136: PRO184, represented by seq.ID.s 281 and 282, (PRO185 skipped; follows below)

Invention 137: PRO200, represented by seq.ID.s 285 and 286, (PRO202 skipped; follows below)

Invention 138: PRO214, represented by seq.ID.s 289 and 290, (PRO215 skipped; follows below)

Invention 139: PRO219, represented by seq.ID.s 293 and 294, (PRO211 skipped; follows below)

Invention 140: PRO220, represented by seq.ID.s 297 and 298, (PRO366, PRO216, PRO221 skipped; follows below)

Invention 141: PRO228, represented by seq.ID.s 305 and 306,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

(PRO217, PRO222, PRO224 skipped: follows below)
Invention 142: PRO230, represented by seq.ID.s 313 and 314,
(PRO198 skipped: follows below)
Invention 143: PRO226, represented by seq.ID.s 317 and 318,
...
Invention 151: PRO323, represented by seq.ID.s 333 and 334,
(PRO245 skipped: follows below)
Invention 152: PRO246, represented by seq.ID.s 337 and 338,
...
Invention 155: PRO257, represented by seq.ID.s 343 and 344,
(PRO172 skipped: follows below)
Invention 156: PRO258, represented by seq.ID.s 347 and 348,
(PRO265 skipped: follows below)
Invention 157: PRO326, represented by seq.ID.s 351 and 352,
(PRO266 skipped: follows below)
Invention 158: PRO269, represented by seq.ID.s 355 and 356,
...

Invention 160: PRO328, represented by seq.ID.s 359 and 360,
(PRO344 skipped: follows below)
Invention 161: PRO272, represented by seq.ID.s 363 and 364,
(PRO301 skipped: follows below)
Invention 162: PRO331, represented by seq.ID.s 367 and 368,
...
Invention 165: PRO310, represented by seq.ID.s 373 and 374,
(PRO337 skipped: follows below)
Invention 166: PRO346, represented by seq.ID.s 377 and 378,
Invention 167: PRO350, represented by seq.ID.s 379 and 380,
(PRO526 skipped: follows below)
Invention 168: PRO381, represented by seq.ID.s 383 and 384,
...
Invention 173: PRO731, represented by seq.ID.s 393 and 394,
(PRO322 skipped: follows below)
Invention 174: PRO536, represented by seq.ID.s 397 and 398,
(PRO719 skipped: follows below)
Invention 175: PR0619, represented by seq.ID.s 401 and 402,
...
Invention 214: PRO1475, represented by seq.ID.s 479 and 480,
(PRO1312 skipped: follows below)
Invention 215: PRO1308, represented by seq.ID.s 483 and 484,
...
Invention 222: PRO1358, represented by seq.ID.s 497 and 498,
(PRO1286 skipped: follows below)
Invention 223: PRO1294, represented by seq.ID.s 501 and 502,
Invention 224: PRO1273, represented by seq.ID.s 503 and 504,
(PRO1279 skipped: follows below)
Invention 225: PRO1195, represented by seq.ID.s 507 and 508,
Invention 226: PRO1271, represented by seq.ID.s 509 and 510,
(PRO1338, PRO1343 skipped: follows below)
Invention 227: PRO1434, represented by seq.ID.s 513 and 514,
...
Invention 237: PRO1693, represented by seq.ID.s 536 and 537,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

(PRO1868 skipped: follows below)

Invention 238: PRO1890, represented by seq.ID.s 539 and 540,

...

Invention 240: PRO4353, represented by seq.ID.s 543 and 544,
(PRO1801 skipped: follows below)

Invention 241: PRO4357, represented by seq.ID.s 547 and 548,

Invention 242: PRO4302, represented by seq.ID.s 549 and 550.

For the sake of conciseness, the first subject matter is explicitly defined, the subject matter of inventions 2-241 are defined by analogy thereto, whereby the numbering of the sequences is followed, except for sequences which are mentioned in one of claims 21-68; inventions relating thereto follow below.

Invention 243: claims 43-49, 53, 54 completely,
and claims 1-24, 29-31, 35, 36, 69-71,
all partially

PRO1114: nucleic acid with seq.ID.31, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.32 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.32 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1801 and/or PRO100 using their interactions with PRO1114, method for linking a bioactive molecule to a cell expressing PRO1801 and/or PRO100 through the use of PRO1114, and method of modulating at least one activity of said cell thereby.

Invention 244: claims 1-24, 29-31, 35, 36, 53, 54,
69-71, all partially

PRO4978: nucleic acid with seq.ID.187, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.188 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.188 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1801 using its interaction with PRO4978, method for linking a bioactive molecule to a cell expressing PRO1801 through the use of

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

PRO4978, and method of modulating at least one activity of said cell thereby.

Invention 245: claims 39-42, 50-52, 55, 56 completely, and claims 1-20, 69-71, all partially

PRO100: nucleic acid with seq.ID.219, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.220 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.220 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1801 and/or PRO1114 using their interactions with PRO100, method for linking a bioactive molecule to a cell expressing PRO1801 and/or PRO1114 through the use of PRO100, and method of modulating at least one activity of said cell thereby.

Invention 246: claims 1-20, 57, 69-71, all partially

PRO195: nucleic acid with seq.ID.271, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.272 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.272 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO195 protein.

Invention 247: claim 66 completely, and claims 1-20, 58, 59, 69-71, all partially

PRO182: nucleic acid with seq.ID.275, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.276 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.276 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for inhibiting the binding of A-peptide to factor VIIA using the PRO182 protein.

Invention 248: claims 1-20, 67, 69-71,
all partially

PRO185: nucleic acid with seq.ID.283, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.284 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.284 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for inhibiting the differentiation of adipocytes using the PRO185 protein.

Invention 249: claims 1-20, 57, 59, 60, 69-71,
all partially

PRO202: nucleic acid with seq.ID.287, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.288 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.288 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for stimulating the proliferation or differentiation of chondrocytes, and method for modulating the uptake of glucose or FFA by adipocytes using the PRO202 protein.

Invention 250: claims 1-20, 57, 69-71,
all partially

PRO215: nucleic acid with seq.ID.291, encoding a polypeptide comprising the amino acid sequence as represented in

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

seq.ID.292 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.292 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO215 protein.

Invention 251: claims 1-20, 60, 69-71,
all partially

PRO211: nucleic acid with seq.ID.295, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.296 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.296 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by adipocytes using the PRO211 protein.

Invention 252: claim 61 completely,
and claims 1-20, 58, 59, 69-71, all partially

PRO366: nucleic acid with seq.ID.299, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.300 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.300 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for stimulating the proliferation of gene expression in pericytes using the PRO366 protein.

Invention 253: claim 62 completely,
and claims 1-20, 69-71, all partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

PRO216: nucleic acid with seq.ID.301, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.302 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.302 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of proteoglycans from cartilage using the PRO216 protein.

Invention 254: claims 1-20, 57, 69-71,
all partially

PRO221: nucleic acid with seq.ID.303, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.304 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.304 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO221 protein.

Invention 255: claims 1-20, 69-71, all partially

PRO217: nucleic acid with seq.ID.307, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.308 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.308 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO217 protein.

Invention 256: claim 68 completely,
and claims 1-20, 69-71, all partially

PRO222: nucleic acid with seq.ID.309, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.310 or a nucleic acid having at least 80% homology

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.310 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, and method for stimulating the proliferation of endothelial cells using the PRO222 protein.

Invention 257: claims 1-20, 59, 69-71,
all partially

PRO224: nucleic acid with seq.ID.311, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.312 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.312 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, and method for stimulating the proliferation or differentiation of chondrocytes using the PRO224 protein.

Invention 258: claims 1-20, 57-59, 67, 69-71,
all partially

PRO198: nucleic acid with seq.ID.315, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.316 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.316 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for inhibiting the differentiation of adipocytes using the PRO198 protein.

Invention 259: claims 1-20, 57, 69-71,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

all partially

PRO245: nucleic acid with seq.ID.335, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.336 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.336 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO245 protein.

Invention 260: claim 63 completely,
and claims 1-20, 57-59 69-71, all partially

PRO172: nucleic acid with seq.ID.345, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.346 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.346 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for modulating the uptake of glucose or FFA by skeletal cells, method for stimulating the proliferation or differentiation of chondrocytes, and method for stimulating the proliferation of inner ear utricular supporting cells using the PRO172 protein.

Invention 261: claims 1-20, 57, 69-71,
all partially

PRO265: nucleic acid with seq.ID.349, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.350 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.350 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO265 protein.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 262: claims 1-20, 57, 69-71,
all partially

PRO266: nucleic acid with seq.ID.353, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.354 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.354 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO266 protein.

Invention 263: claim 64 completely,
and claims 1-20, 57, 60, 69-71, all partially

PRO344: nucleic acid with seq.ID.361, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.362 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.362 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, method for modulating the uptake of glucose or FFA by adipocytes, and method for stimulating the proliferation of T-lymphocytes using the PRO344 protein.

Invention 264: claims 1-20, 59, 69-71,
all partially

PRO301: nucleic acid with seq.ID.365, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.366 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.366 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the proliferation

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

or differentiation of chondrocytes using the PR0301 protein.

Invention 265: claims 1-20, 57, 69-71,
all partially

PR0337: nucleic acid with seq.ID.375, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.376 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.376 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PR0337 protein.

Invention 266: claims 1-20, 65, 69-71,
all partially

PR0526: nucleic acid with seq.ID.381, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.382 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.382 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of a cytokine from PBMC cells using the PR0526 protein.

Invention 267: claims 1-20, 57, 69-71,
all partially

PR0322: nucleic acid with seq.ID.395, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.396 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.396 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PR0322 protein.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 268: claims 1-20, 58, 69-71,
all partially

PRO719: nucleic acid with seq.ID.399, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.400 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.400 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for modulating the uptake of glucose or FFA by skeletal cells using the PRO719 protein.

Invention 269: claims 1-20, 59, 69-71,
all partially

PRO1312: nucleic acid with seq.ID.481, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.482 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.482 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the proliferation or differentiation of chondrocytes using the PRO1312 protein.

Invention 270: claims 1-20, 57, 69-71,
all partially

PRO1286: nucleic acid with seq.ID.499, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.501 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.501 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO1286 protein.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 271: claims 1-20, 57, 69-71,
all partially

PRO1279: nucleic acid with seq.ID.505, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.506 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.506 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood using the PRO1279 protein.

Invention 272: claims 1-20, 57, 60, 69-71,
all partially

PRO1338: nucleic acid with seq.ID.511, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.512 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.512 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of TNF-alpha from human blood, and method for modulating the uptake of glucose or FFA by adipocytes using the PRO1338 protein.

Invention 273: claims 1-20, 57, 65, 69-71,
all partially

PRO1343: nucleic acid with seq.ID.513, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.514 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.514 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the release of

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

TNF-alpha from human blood, and method for stimulating the release of a cytokine from PBMC cells using the PRO1343 protein.

Invention 274: claims 1-20, 59, 69-71,
all partially

PRO1868: nucleic acid with seq.ID.537, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.538 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.538 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also method for stimulating the proliferation or differentiation of chondrocytes using the PRO1868 protein.

Invention 275: claims 25-28, 32-34, 37,
38 completely, and claims 1-20, 69-71,
all partially

PRO1801: nucleic acid with seq.ID.545, encoding a polypeptide comprising the amino acid sequence as represented in seq.ID.546 or a nucleic acid having at least 80% homology thereto, vector comprising said nucleic acid, host cell comprising said vector, process for producing the protein of seq.ID.546 using said host, the isolated protein or one having at least 80% homology thereto, a chimeric protein of said peptide fused to a heterologous sequence, isolated extracellular domain of said protein or said protein lacking its signal peptide, and an antibody against said polypeptide. Also a method of detecting PRO1114 and/or PRO4978 using its interaction with PRO1801, method for linking a bioactive molecule to a cell expressing PRO4978 and/or PRO1114 through the use of PRO1801, and method of modulating at least one activity of said cell thereby.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte: International Application No

PCT/US 00/32678

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 9821328	A 22-05-1998	AU EP WO	4885297 A 0941320 A2 9821328 A2	03-06-1998 15-09-1999 22-05-1998
WO 9909061	A 25-02-1999	AU EP WO	9115898 A 0971955 A1 9909061 A1	08-03-1999 19-01-2000 25-02-1999
EP 0834563	A 08-04-1998	EP JP US	0834563 A2 10179178 A 5824504 A	08-04-1998 07-07-1998 20-10-1998
WO 9707198	A 27-02-1997	US AU AU AU AU CA CA EP EP JP US WO WO US US	5707829 A 727480 B2 6712396 A 727489 B2 6768596 A 2227220 A1 2229208 A1 0839196 A2 0851875 A2 11510045 T 6043344 A 9704097 A2 9707198 A2 6074849 A 5969093 A	13-01-1998 14-12-2000 18-02-1997 14-12-2000 12-03-1997 06-02-1997 27-02-1997 06-05-1998 08-07-1998 07-09-1999 28-03-2000 06-02-1997 27-02-1997 13-06-2000 19-10-1999
WO 0037630	A 29-06-2000	AU EP WO	2390800 A 1141267 A1 0037630 A1	12-07-2000 10-10-2001 29-06-2000